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A convenient synthesis of 8,8′-spiro-bi(chromano-1,2-oxaphosphinine) derivatives

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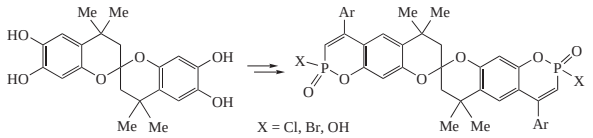
8,8′-Spirobi(chromano-1,2-oxaphosphinines) were obtained by the reaction between phosphorylated derivatives of spirodichromane and arylacetylenes with a high chemoselectivity.



Spirocyclic polyhydroxyarenes of chromane series are a special group of polyphenolic compounds that possess a broad spectrum of practically important properties. Spirocyclic compounds have nonlinear structures and comprise rigidly bound annular moieties, owing to which they can be used to obtain polymeric and supramolecular compounds with various structures.[1–5] Low-molecular spirochromane derivatives containing chromophoric groups form 3D holographic gratings and can be employed to create holographic data storage systems.[6]

Incorporation of four hydroxy groups, which form two catechol systems, into the spirochromane structure opens the way to phosphacoumarin (areno-1,2-oxaphosphinine) derivatives.[7] The structural similarity of this class of compounds to natural coumarins and the presence of a phosphorus atom predetermine the biological activity of phosphacoumarins and phosphaisocoumarins. For example, Li *et al.*[8] performed a rather comprehensive study of the inhibiting effect of phosphorus-containing compounds with isocoumarin structure on the activity of cholesterol esterase.

In this study, we suggest an easy and efficient access to 8,8′-spirobi(chromano[6,7-*e*]-1,2-oxaphosphinines) based on the reaction of phosphorylated derivatives of 6,6′,7,7′-tetrahydroxy-4,4,4′,4′-tetramethyl-2,2′-spirobichromane **1** with acetylenes. The starting spirochromane **1** was obtained by condensation of 1,2,4-triacetoxybenzene with acetone in the presence of acetic and hydrochloric acids.[9] The structure of the resulting tetraol was confirmed by spectral methods (^{1}H NMR spectroscopy, mass spectrometry).

It is known that polyhydroxyarenes are poorly soluble in most organic solvents. For this reason, tetraol **1** was converted to silyl ether **2** by the reaction with excess chlorotrimethylsilane in the presence of triethylamine (Scheme 1).† Compound **2** is a dark oily liquid well soluble in dichloromethane. Further, silyl ether **2** was treated with a phosphorus trihalide taken in excess.‡ The phosphorylation occurs under mild conditions to give phosphites **3a**,**b** in high yields. According to ^{31}P NMR data, the content of compounds **3a**,**b** in the reaction mixture was 90–95%. It should also be noted that compound **3a** manifests itself in the ^{31}P-{^{1}H}NMR spectrum as two closely-spaced singlets (δ_P 198.6 and 199.5) in 7.9 : 1 ratio. This suggests that stereoisomers exist, possibly with different orientations of the halogen atoms.

Halophosphites **3a**,**b** were converted to chloro- and bromophosphoranes **4a**,**b** by the reactions with phosphorus pentachloride and molecular bromine, respectively (see Scheme 1).§ Analysis of

† *6,6′,7,7′-Tetrakis(trimethylsiloxy)-4,4,4′,4′-tetramethyl-2,2′-spirobichromane* **2**. A solution of chlorotrimethylsilane (2.9 ml, 23 mmol) in benzene (15 ml) was added dropwise to a solution of spiro chromane **1** (2.18 g, 5.8 mmol) and NEt_3 (3.2 ml, 23 mmol) in 100 ml of absolute benzene. The mixture was stirred at room temperature for 0.5 h. Further, the mixture was heated up to 90 °C and stirred for 1.5 h. On the next day, the mixture was filtered and the solvent was removed *in vacuo*. The residue was a dark oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.21 (s, 18H, $SiMe_3$), 0.25 (s, 18H, $SiMe_3$), 1.32 (s, 6H, Me), 1.53 (s, 6H, Me), 1.94 (d, 2H, CH_2, ^2J 13.9 Hz), 2.07 (d, 2H, CH_2, ^2J 13.9 Hz), 6.15 (s, 2H, H^8), 6.76 (s, 2H, H^5).

‡ *2,2′-Dichloro-8,8,8′,8′-tetramethyl-6,6′-spirobi(chromano[6,7-*d*]-1,3,2-dioxaphosphole)* **3a**. A solution of compound **2** (2.64 g, 4 mmol) in chloroform (15 ml) was added to a solution of phosphorus trichloride (2.0 ml, 23 mmol) in chloroform (10 ml). The mixture was stirred at room temperature for 1.5 h. The solvent and volatile compounds were removed *in vacuo* (12 Torr). Crystalline precipitate of compound **3a** was formed. Yield 1.8 g (90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.41 (s, 6H, Me), 1.61 (s, 6H, Me), 2.01 (br. d, 2H, two A-parts of two AB-spectra, $^2J_{AB}$ 14.0 Hz), 2.15 (br. d, 2H, two B-parts of two AB-spectra, $^2J_{AB}$ 14.1 Hz), 6.59 (br. s, 2H, HC^9), 7.22 (br. s, 2H, HC^4). ^{31}P-{^{1}H} NMR (162 MHz, $CDCl_3$) δ_P: 176.4 (s).

*2,2′-Dibromo-8,8,8′,8′-tetramethyl-6,6′-spirobi(chromano[6,7-*d*]-1,3,2-dioxaphosphole)* **3b**. A solution of compound **2** (3.83 g, 5.8 mmol) in chloroform (15 ml) was added to a solution of phosphorus tribromide (2.2 ml, 23 mmol) in chloroform (5 ml). The reaction mixture was stirred at room temperature for 1.5 h. Crystalline precipitate of compound **3b** was formed, mp 208 °C, yield **3g** (89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.44 (br. s, 6H, Me), 1.63 (br. s, 6H, Me), 2.05 (br. d, 2H, two A-parts of two AB-spectra, $^2J_{AB}$ 14.1 Hz), 2.16 (br. d, 2H, two B-parts of two AB-spectra, $^2J_{AB}$ 14.1 Hz), 6.61 (br. s, 2H, H^8), 7.25 (br. s, 2H, H^5). ^{31}P NMR (162 MHz, CCl_4) δ_P: 198.6 (s), 199.5 (s).

§ *2,2,2,2′,2′,2′-Hexachloro-8,8,8′,8′-tetramethyl-6,6′-spirobi(chromano-[6,7-*d*]-1,3,2-dioxaphosphole)* **4a**. A solution of compound **3a** (1 g, 2 mmol) in dichloromethane (10 ml) was added to a suspension of phosphorus pentachloride (0.83 g, 4 mmol) in dichloromethane (10 ml). The reaction mixture was stirred at room temperature for 2 h at room temperature until complete dissolution of phosphorus pentachloride. The solvent and volatile compounds were removed *in vacuo* (12 Torr). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.35 (s, 6H, Me), 1.57 (s, 6H, Me), 1.99 (d, 2H, two A-parts of two AB-spectra, $^2J_{AB}$ 14.0 Hz), 2.12 (d, 2H, two B-parts of two AB-spectra, $^2J_{AB}$ 14.0 Hz), 6.40 (br. s, 2H, H^9), 7.08 (br. s, 2H, H^4). ^{31}P-{^{1}H} NMR (162 MHz, $CDCl_3$) δ_P: –25.7 (s).

*2,2,2,2′,2′,2′-Hexabromo-8,8,8′,8′-tetramethyl-6,6′-spirobi(chromano-[6,7-*d*]-1,3,2-dioxaphosphole)* **4b**. Bromine (0.6 ml, 12 mmol) was added to a cooled (–20 °C) solution of compound **3b** (3.54 g, 6 mmol) in dichloromethane (15 ml). The orange precipitate was obtained. ^{31}P-{^{1}H} NMR (162 MHz, CH_2Cl_2) δ_P: –189.0 (br. s).